## **REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

All amendments made at this time are corrections and deletions within the scope of the previous claims, and do not introduce new matter.

Claim 10 has been deleted by the above-mentioned amendments. Therefore, the rejection under 35 USC 112, second paragraph is overcome.

The Examiner states that claims 1, 10-12, 19-21, 23 and 24 are rejected under 35 USC 102 as anticipated by Tsai.

The Applicants have incorporated the index of claim 6, free of this rejection, into claim 1 by the above-mentioned amendments. The amended claim 1 is referred to by claims 11, 12 and 19-21. In addition, claims 10, 23 and 24 have been deleted.

Therefore, the Applicants believe that the rejection of these claims under 35 USC 102(b) is overcome.

The Examiner states that claims 2-9, 13, 16, 18, 22 and 25-28 are rejected under 35 USC 103 as obvious over Tsai.

The Applicants have amended the claims to incorporate the index of claim 6 into claim 1, and the other claims to be dependent on the amended claim 1.

The Examiner's holding regarding the present claim 6 is that Tsai is silent on use of an index comparing D-serine concentration to total serine concentration, and that it would have been obvious to one of ordinary skill in the art at the time of invention to uncover the possibility that skewed values of D-serine in affected individuals are attributable to skewed values of total serine which would affect absolute levels of D-serine through the racemase (see Official Action, page 5).

The Examiner's holding is quite appropriate. Snyder (Neurochemical Research, Vol. 25(5), 2000, pp. 553-560) cited by the Examiner teaches that serine racemase has a function not only to convert L-serine to D-serine but also to convert D-serine to L-serine (see the description

from the 10<sup>th</sup> line from the bottom in the right column on page 556). Therefore, D-serine is in equilibrium with L-serine, which means, for example, when the level of D-serine <u>decreases</u>, the level of L-serine also decreases.

However, the present inventors have found a surprising fact, that a D-serine concentration in patients with schizophrenia is <u>lower</u> than in healthy individuals, and conversely, an L-serine concentration in patients with schizophrenia is <u>higher</u> than in healthy persons. Thus, the D-serine concentration in patients with schizophrenia is significantly lower than in healthy persons. Furthermore, the ratio of the D-serine concentration to the total serine concentration in patients with schizophrenia is far significantly lower than in healthy persons. This means that the diagnosis of schizophrenia using the ratio of the D-serine concentration to the total serine concentration is far more accurate than the diagnosis based on the D-serine concentration. Such striking effect is not suggested to those skilled in the art from the aforementioned prior art. Although the Examiner considers diagnosis using the D-serine concentration to be obvious to those skilled in the art, the diagnosis using the ratio of the D-serine concentration to the total serine concentration is not obvious for the foregoing reasons.

Therefore, the Applicants believe that the amended claim 1 and all claims dependent upon claim 1 are unobvious and patentable over the prior art.

In view of the foregoing, it is believed that each ground of rejection set forth in the Official Action has been overcome, and that the application is now in condition for allowance. Accordingly, such allowance is solicited.

Respectfully submitted,

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